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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/595,684	05/04/2006	Andreas Hefel	RBL0109-01	7978
832 7590 11/01/2010 BAKER & DANIELS LLP 111 E. WAYNE STREET SUITE 800 FORT WAYNE, IN 46802			EXAMINER MI, QIUWEN	
			ART UNIT 1655	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

## Application No.

10/595,684

## Applicant(s)

HEFEL, ANDREAS

## Examiner

QIUWEN MI

## Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 22-24, 28 and 31-45 is/are pending in the application.
- 4a) Of the above claim(s) 23, 24, 28 and 31-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22, 44 and 45 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 May 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

Applicant's amendment in the reply filed on 10/20/2010 is acknowledged, with the the additional newly added Claim 45. Claims 22-24, 28, and 31-45 are pending. Claims 23, 24, 28, and 31-43 are withdrawn from further consideration. **Claims 22, 44, and 45 are examined on the merits.**

Any rejection that is not reiterated is hereby withdrawn.

#### Claim Rejections –35 USC § 112, 1<sup>st</sup> New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 45 is newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

This is a new rejection necessitated by the Applicant's amendment filed on 10/20/2010.

Claim 45 recites "The procedure of claim 22, wherein said first granule does not include a hydrophobic material". However, the specification fails to provide any support regarding the "the first granule does not include a hydrophobic material". First of all, there is no recitation of "first granule" in claim 22. Secondly, claim 22 recites "the nutritional additive in the granulate" in lines 17-18, and "the nutritional additive" is selected from "fat-soluble vitamins" etc, and "fat-soluble vitamins" are hydrophobic materials, thus the granulate does include hydrophobic

materials. Therefore, it is not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, Applicant had possession of the “the first granule does not include a hydrophobic material” in the invention. Thus, the subject matter of “the first granule does not include a hydrophobic material” is a new matter that needs to be cancelled.

### **Claim Rejections –35 USC § 112, 2<sup>nd</sup>**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22 and 44 remain rejected, claim 45 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 6/11/2010, repeated below, slightly altered to take into consideration Applicant’s amendment filed on 10/20/2010. Applicants’ arguments filed have been fully considered but they are not deemed to be persuasive.

Claim 22 recites “at least one nutritional additive selected from the group consisting of herbal extracts, water-soluble vitamins, fat-soluble vitamins, amino acids, fatty acids, minerals, and hormones, mixed carotenoids, co-enzyme Q10, lycopenes, lutein, zeaxanthin, bioflavonoids, germanium, selenium, zinc, vitamin A, vitamin C, vitamin E, alpha-Lipoic, grape sperm-seed phytosome, extract from green tea and extract from pine bark, ...” (lines 9-15). The

recitation is very confusing. First of all, vitamin A and vitamin E are fat-soluble vitamins; and vitamin C is water-soluble vitamin. Secondly, "extract from green tea and extract from pine bark" falls into the category of "herbal extracts". Thirdly, "selenium and zinc" falls into the category of "minerals". Regarding the recitation of "alpha-lipoic" at line 14, it is not clear whether Applicant refers to "alpha lipoic acid".

Claim 22 recites "a first hormone" in line 4, and claim 22 recites "minerals and hormones" in line 11. It is not clear whether the "hormones" in line 11 includes the "first hormone" or not.

Further more, the recitation of "the nutritional additive in the granulate" in lines 17-18 is very confusing, as "samatotropin is mixed with the galactomannan and/or glucomannan before granulation", thus it is not clear how the nutritional additive is in the granulate as well.

Claim 45 recites "The procedure of claim 22, wherein said first granule does not include a hydrophobic material". The recitation "said first granule" is confusing, as there is insufficient antecedent basis for the limitation in claim 22.

Therefore, the metes and bounds of claims are rendered vague and indefinite. The lack of clarity renders the claims very confusing and ambiguous since the resulting claims do not clearly set forth the metes and bounds of the patent protection desired.

All other cited claims depend directly or indirectly from rejected claims and are, therefore, also, rejected under U.S.C. 112, second paragraph for the reasons set forth above.

**Claim Rejections –35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 22 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Baichwal (WO 97/26865), in view of Kim et al (KR 143767 B1).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 6/11/2010, repeated below, slightly altered to take into consideration Applicant's amendment filed on 10/12/2010. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

Baichwal teaches a sustained-release formulation (thus increase of the nutrient-bio-availability of vital substances in a human or an animal) for use in oral solid dosage forms includes from about 10 to about 40 percent or more by weight galactomannan gum; from about 1 to about 20 percent by weight of an ionizable gel strength enhancing agent and an inert pharmaceutical filter (see Abstract). Baichwal also teaches in certain preferred embodiments for the invention, the sustained release matrix further comprises a hydrophobic material in an amount effective to slow the hydration of the gum without disrupting the hydrophilic matrix formed by the homopolysaccharide when the formulation is exposed to fluids in an environment of use. This may be accomplished by granulating the sustained release matrix prior to the

incorporation for the medicament (thus are embedded in a botanical matrix of a botanical matrix of a polysaccharide). The hydrophobic material may be selected from alkylcelluloses, acrylic and/or methacrylic acid polymers or copolymers, hydrophobic vegetable oils (thus herbal extracts; thus at least one nutritional additive), zein, as well as other pharmaceutically acceptable hydrophobic materials known to those skilled in the art (page 9, lines 9-22). Baichwal also teaches the homopolysaccharide gums used in the present invention include the galactomannan, i.e. polysaccharides which are composed solely of mannose and galactose. Galactomannans which have higher proportions of unsubstituted mannose are preferred in certain embodiments. Locust bean gum, which has a higher ratio of mannose to the galactose, is especially preferred as compared to other galactomannans such as guar and hydroxypropyl guar (page 6, lines 13-18) (thus are embedded in a botanical matrix of a botanical matrix of a polysaccharide). Baichwal further teaches accordingly, the ingredients of the sustained release pharmaceutical excipient prepared in accordance with the present invention may be subjected to wet granulation before the medicament is added (thus somatotropin, the nutritional additive and the antioxidant in the granulate do that interact with one another; thus the granulate swells in a digest system of a human or an animal slowly releasing a nutritiously active quantity of said somatotropin, the nutritional additive, and the antioxidant for absorption by the human or animal digestive system). In this technique, the desired amounts of the homopolysaccharide, the ionizable gel strength enhancing agent, and the inert filler are mixed together and thereafter a moistening agent such as water, propylene glycol, glycerol, alcohol or the like is added to prepare a moistened mass. Next, the moistened mass is dried. The dried mass is then milled with conventional equipment product is ready to use. The granulate thus obtained has certain advantages including the fact that it is

free-flowing, has good cohesive properties, and can be admixed with an active agent (e.g., drug) (thus somatotropin, the nutritional additive and the antioxidant in the granulate do that interact with one another) and can be directly compressed into tablets (page 11, lines 7-23). Baichwal teaches alternatively, the medicament may be wet-granulated in appropriate circumstance with one or more of the ingredients of the sustained release excipient. The remaining release excipient ingredients can simply be admixed to the resultant pre-granulated material (thus a first hormone is mixed with the galactomannan and/or a glucomannan before granulation) or granulated together with the pre-granulated ingredients (thus somatotropin, the nutritional additive and the antioxidant in the granulate do that interact with one another) in a second wet granulation step (page 12, lines 3-9) (thus the granulates swells in a digest system of a human or an animal slowly releasing a nutritiously active quantity of said somatotropin, the nutritional additive and the antioxidant for absorption by the human or animal digestive system). Baichwal further teaches finally, in further alternative embodiments of the invention, a therapeutically active agent can be incorporated (admixed, granulated, etc.) with any of the ingredients of the sustained release excipient, if so desired (page 13, lines 24-30). Baichwal at last teaches examples of such therapeutically active agents include hormones (e.g., insulin, heparin), vitamins etc (thus at least one antioxidant) (page 16, last paragraph bridging page 17).

Baichwal does not teach explicitly somatotropin is embedded in galactomannan and/or glucomannan.

Kim et al teach an implantable formula containing somatotropin is provided for sustained release of somatotropin that promotes animal's growth. A process for the preparation of sustained releasing formula containing somatotropin comprises of: mixing polyethylene



glycol, the water-soluble polymer with somatotropin or liposome bovine somatotropin; adding some water and mixing; granulation; coating granulated compd. by spraying hydroxyl Pr cellulose dissolved in ethanol using spray gun; making tablet or pellet by tablet machine (see Abstract, machine translation is attached).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to embed somatotropin human growth hormone in a galactomannan and/or a glucomannan since Baichwal teaches embedding therapeutically active agents such as hormones in sustained-release granulate containing galactomannan gum; Kim et al teach somatotropin in a sustained-release granulate; therefore, one of the ordinary skills in the art would have been motivated to embed somatotropin human growth hormone in a galactomannan and/or a glucomannan. Since both of the references teach granulation of sustain release hormone, one of ordinary skill in the art would have been motivated to combine the teachings of the references together.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Claims 22 and 44 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Baichwal and Kim et al as applied to claim 22 above, and further in view of Shefer et al (US 2003/0195133).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 6/11/2010, repeated below, slightly altered to take into consideration Applicant's amendment filed on 10/12/2010. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

The teachings of Baichwal and Kim et al are set forth above and applied as before.

The combination of Baichwal and Kim et al does not specifically teach the nutritional material comprises antioxidant coenzyme Q10.

Shefer et al teach controlled delivery composition (see Title). Shefer et al teach the controlled release system of the invention can also contain other antioxidants including those well known in the art. Representative antioxidants include vitamin E, tocopheryl acetate, betaglukan, and coenzyme Q10 [0136].

It would also have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to adopt the procedure of using antioxidant coenzyme Q10, or vitamin E in the slowly released/control released system since Shefer et al teach the controlled release system of the invention can also contain antioxidants coenzyme Q10 or vitamin E. Furthermore, since Baichwal teaches galactomannan and/or a glucomannan allowing sustainment of pharmacological effect of a variety of active ingredients administered to mammals, one of ordinary skill in the art would have adopted the procedure of using glucomannan to sustain the pharmacological effect of antioxidant coenzyme Q10, or vitamin E.

Since all the references yielded beneficial results in sustained release system, one of ordinary skill in the art would have been motivated to combine the teachings of the references together.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Applicant argues that "The primary reference relied upon in the obviousness rejection of claim 22 is Baichwal. The Action recites that certain preferred embodiments of Baichwal's teaches that, " ... the sustained release matrix further comprises a *hydrophobic material in an* amount effective to slow the hydration of the gum without disrupting the hydrophobic matrix formed by the homopolysaccharide when the formation is exposed to fluids in an environment of use. This maybe accomplished by granulating the sustained release matrix *prior to the incorporation for the medicament* (thus are embedded in a botanical matrix of a botanical matrix of polysaccharide)," Action, page 4, second full paragraph (emphasis added), The only examples in Baichwal teach forming granules that include both a source of polysaccharide (in these examples locust Bean Gum) and a hydrophobic material (in these examples calcium calcium sulfate) *before a medicament is added to granule*, Examples 1-3 pages 19-20 (page 5, last paragraph bridging page 6).

This is not found persuasive. There is no recitation of "hydrophobic material" in claim 22.

Applicant argues that "In contrast to the preferred and exemplified embodiments of Baichwal the applicants' claimed invention comprises a mixture of granules one of which

includes somatotropin incorporated into the matrix of a polysaccharide before the granule is formed by drying the mixture. All three of the Examples in the instant application teach mixing a bioactive ingredient with a polysaccharide and then drying the resulting mixture to form a solid which is finally milled to form the final granule. Moreover none of the granules exemplified in the instant application include the addition of a hydrophobic material... Examples 1-3, paragraphs [0026] to [0028]" (page 6, 2<sup>nd</sup> paragraph).

This is not found persuasive. Claim 22 recites "the nutritional additive in the granulate" in lines 17-18, and "the nutritional additive" is selected from "fat-soluble vitamins" etc, and "fat-soluble vitamins" are hydrophobic materials, thus the granulate in the current application does include hydrophobic materials.

Applicant argues that "As noted in the Action, Baichwal mentions that, "... the medicament may be wet-granulated *in appropriate circumstances* with one or more of the ingredients of the sustained release excipient. The remaining release excipient ingredients can simply be admixed to the resultant pre-granulated material or granulated together with the pre-granulated ingredients ...". See Action, pages 5-6 citing to Baichwal page 12, lines 3-9, emphasis added. Despite this language in Baichwal, none of the examples in Baichwal illustrate making or using such a formation. The lack of examples and other guidance concerning 'wet granulation' of medicaments mid a polysaccharide formulation illustrates that type of granule is not enabled. The only guidance provided by Baichwal in this regard is that granules in which the medicament is added before granulation may be formed in appropriate circumstance. Neither Baichwal nor any of the other references cited by the office offer any useful guidance as to what constitutes appropriate circumstances. One of ordinary skill in the art having knowledge of Baichwal would

have to engage in extensive experimentation in order to arrive at the applicants' claimed invention, in this regard, the disclosure of Baichwal is an invitation to undue experimentation and does not render claim 22 obvious" (page 6, 3<sup>rd</sup> paragraph).

This is not found persuasive. Baichwal further teaches accordingly, the ingredients of the sustained release pharmaceutical excipient prepared in accordance with the present invention may be subjected to wet granulation before the medicament is added. In this technique, the desired amounts of the homopolysaccharide, the ionizable gel strength enhancing agent, and the inert filler are mixed together and thereafter a moistening agent such as water, propylene glycol, glycerol, alcohol or the like is added to prepare a moistened mass. Next, the moistened mass is dried. The dried mass is then milled with conventional equipment product is ready to use. The granulate thus obtained has certain advantages including the fact that it is free-flowing, has good cohesive properties, and can be admixed with an active agent (e.g., drug) and can be directly compressed into tablets (page 11, lines 7-23). Baichwal teaches alternatively, the medicament may be wet-granulated in appropriate circumstance with one or more of the ingredients of the sustained release excipient. The remaining release excipient ingredients can simply be admixed to the resultant pre-granulated material or granulated together with the pre-granulated ingredients in a second wet granulation step (page 12, lines 3-9). Baichwal further teaches finally, in further alternative embodiments of the invention, a therapeutically active agent can be incorporated (admixed, granulated, etc.) with any of the ingredients of the sustained release excipient, if so desired (page 13, lines 24-30). Baichwal at last teaches examples of such therapeutically active agents include hormones (e.g., insulin, heparin), vitamins etc (page 16, last paragraph bridging page 17). Therefore, Baichwal provides sufficient guidance to enable the claimed invention.

Applicant argues that “Nothing in Baichwal teaches forming a granule that does not include a hydrophobic material such as calcium sulfate, in contrast, the applicants' claimed invention does not recite the need for a hydrophobic additive. See Application, examples 1-3, paragraphs [0026] to [0028]. Moreover, as noted in the Action, Baichwal fails to disclose somatotropin. See Action, pg. 6, first full paragraph. Unlike the applicants' claimed invention, Baichwal cannot teach the advantages of associating somatotropin with a polysaccharide matrix formed by mixing somatotropin with the components of a matrix before forming the matrix. Accordingly, nothing disclosed in Baichwal would lead one of ordinary skill to add somatotropin to a mixture of galactomannan and/or a glucomannan before drying the mixture and processing the resulting dry mixture to form granules that include somatotropin associated with the lattice of a polysaccharide” (page 7, 1<sup>st</sup> paragraph).

This is not found persuasive. Claim 22 recites “the nutritional additive in the granulate” in lines 17-18, and “the nutritional additive” is selected from “fat-soluble vitamins” etc, and “fat-soluble vitamins” are hydrophobic materials, thus the granulate in the current application does include hydrophobic materials. In addition, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, there is no recitation of “calcium sulfate” in the claims, thus the argument regarding “calcium sulfate” is not relevant.

Applicant's arguments have been fully considered but they are not persuasive, and therefore the rejections in the record are maintained.

### **Conclusion**

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Qiuwen Mi/

Primary Examiner, Art Unit 1655